

Applicant: MARY ANN D. BROW et al.

Sheet 1 of 6

FORM PTO-1449 (Modified)

U.S. Department of Commerce Patent and Trademark Office

Attorney Docket No.: FORS-06612

Serial No.: 09/940,925

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary)

(37 CFR § 1.	98(b))	(Use Several Sheet			Filing Date: 08/28	/01	Group Art Ur	nit: /63	<u>``(</u>
		· · · · · · · · · · · · · · · · · · ·		U.S. PATENT DOC	CUMENTS				<u></u>
Examiner Initials		Serial / Patent Number	Issue Date	Applic	ant / Patentee	Class	Subclass	Filing	Date
ONP)	1	4,683,195	7/28/87	Mı	ullis <i>et al</i>	485	4	2/7/	′86
	5	4,683,202	7/28/87		Mullis	415	9	10/25	5/85
[A 200;	4	5,108,892	4/28/92	Ві	ırke <i>et al</i>	435	6	8/3/	′89
4/2	<b>4</b> /4	5,144,019	9/1/92	R	ossi <i>et al.</i>	536	27	6/21	/89
RADMARK	5_	4,511,502	4/16/85	Bu	ilder et al.	260	112	6/1/	′84
(1)	6	4,518,526	5/21/85		Olson	260	112	6/1/	′84
BI	7	4,511,503	4/16/85	Ol	son et al.	260	112	6/1/	/84
M	8	4,512,922	4/23/85	Jo	nes et al.	260	112	6/1/	/84
110	9	5,455,170	10/03/95	Abra	imson et al.	415	252.3	8/27	/93
(2)	10	5,614,402	5/25/97	Dah	ilberg et al.	415	199	6/6/	'94
19)	11	5,541,311	7/30/96		ilberg et al.	536	23.7	6/4/	93
10)	12	5,422,253	6/6/95		ilberg et al.	435	91.53	12/7	/92
11/	13	5,422,242	6/6/95		Young	435	6	7./17	
1	,	1_300	OREIGN PATENTS O				100 000		
3)				i i i i i i i i i i i i i i i i i i i	I DON'T I I DON'T THE	Dioxinons -		Transl	ation
0		Document Number	Publication Date	Country	Country / Patent Office	Class	Subclass	Yes	N
181	14	WO 90/01069	2/8/90		PCT	C 2Q	1/68	H	INC
m	15	WO 92/06200	4/16/92	<del></del>	PCT	C12N	15/54	오	
	16	WO 91/09950	7/11/91		PCT	CI2N	15/54	8	JAN
1	17	WO 90/15157	12/13/90	<del></del>	PCT	CI2Q	1/68	111	
m	18	E PO 482 714 A1	4/29/92		EPA	CIPN	15/54		0
	10		DOCUMENTS (Includ	ling Author Title D			1 10:04	<u>ā</u>	200
120	19	· · ·			<del></del>			<u> </u>	<u> </u>
20	<b></b>		isease detection and DI				. Acaa. Sci., 88:	189 (	
1	20_		Barany, "The Ligase Chain Reaction in a PCR World," PCR Methods and Applic., 1:5 (1991);						
	21	Template-Depender	Wu and Wallace, "The Ligation Amplification Reaction (LAR) - Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Ligation," Genomics 4:560 (1989);						
1	22	Guatelli et al., "Isothermal, in vitro amplification of nucleic acids by a multienzyme reaction modeled after retroviral replication," Proc. Natl. Acad. Sci., 87:1874-1878 (1990) with an erratum at Proc. Natl. Acad. Sci., 87:7797 (1990);							
11	23	Kwoh et al., "Transcription-based amplification system and detection of amplified human immunodeficiency virus type 1 with a bead-based sandwich hybridization format," Proc. Natl. Acad. Sci., 86:1173-1177 (1989);							
1	24	Fahy et al., "Self-sustained Sequence Replication (3SR): An Isothermal Transcription-based Amplification System Alternative to PCR," PCR Meth. Appl., 1:25-33 (1991);							
111	25	Landgren, "Molecular mechanics of nucleic acid sequence amplification," Trends in Genetics 9:199 (1993);							
	26	Mullis, "The Polymerase Chain Reaction in an Anemic Mode: How to Avoid Cold Oligodeoxyribonuclear Fusion," PCR Methods Applic., 1:1 (1991);							
				*****					-001-6
<u>n</u>	27		ts of primer-template n ls Res., 18:999 (1990);		olymerase chain reacti	on: Human immuno	deficiency virus	type 1 mode	el
xaminer:	27 4 M	studies," Nucl. Acid			Olymerase chain reacti  Date Considered:	on: Human immuno		type 1 mode	el 

FORM PTO-1449 (Modified)

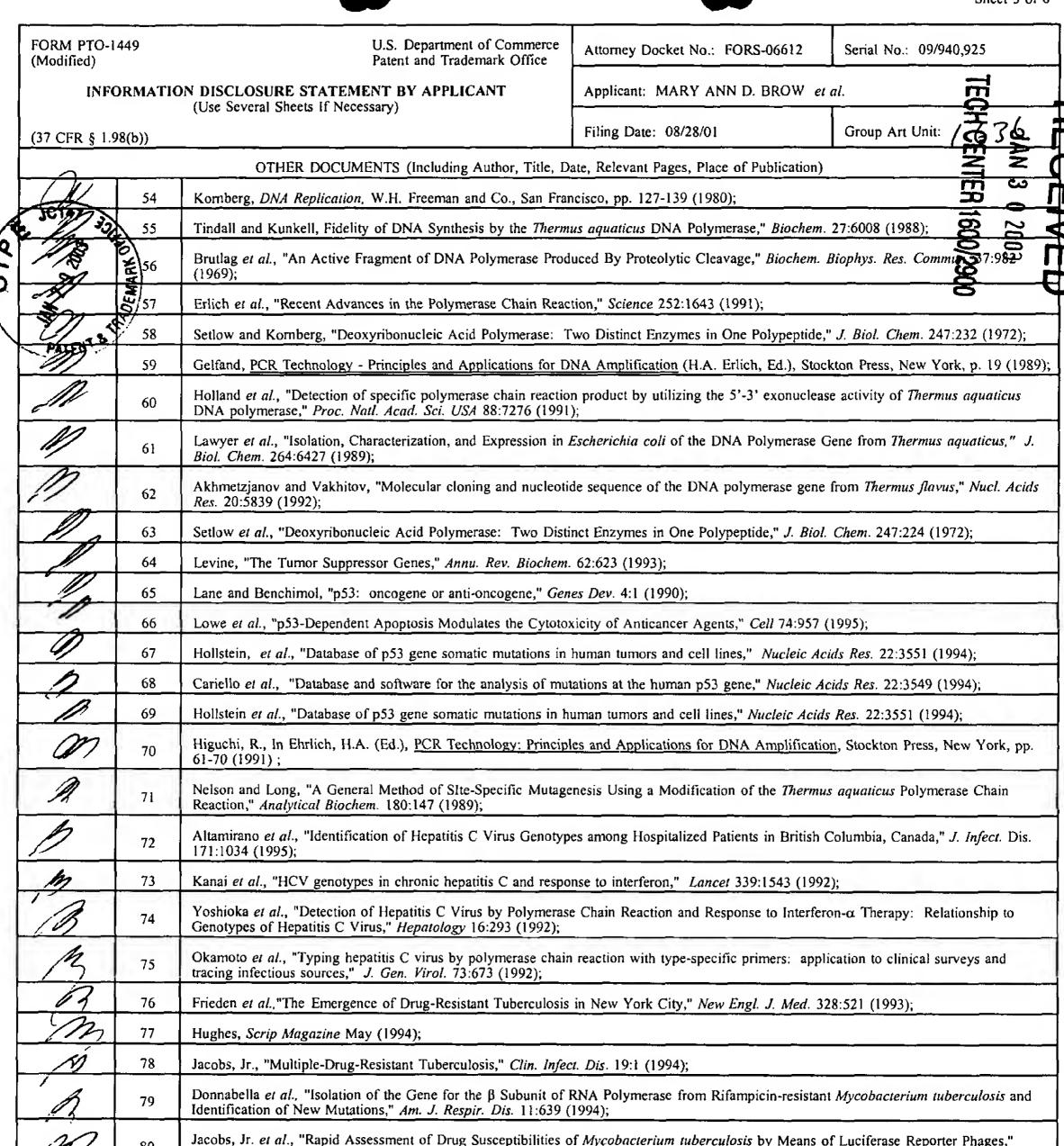
U.S. Department of Commerce Patent and Trademark Office

Attorney Docket No.: FORS-06612

Serial No.: 09/9401225

A

OTHER DOCUMENTS (Including Author, Title, Date, Relevan: Pages, Place of Publication)  OTHER DOCUMENTS (Including Author, Title, Date, Relevan: Pages, Place of Publication)  OTHER DOCUMENTS (Including Author, Title, Date, Relevan: Pages, Place of Publication)  OTHER DOCUMENTS (Including Author, Title, Date, Relevan: Pages, Place of Publication)  Urdea et al., "Probe Amplifier System Based on Chimeric Cycling Oligonucleotides," BioTech., 9:142 (1990);  Urdea et al., "Deceivion of single base instruments of thymine and cytosine residues by polassium permanganue and hydroxylamine in the prese of terrila; Mannenium ansist." Amount of pages at al., "Deceivion of single base instruments of thymine and cytosine residues by polassium permanganue and hydroxylamine in the prese of terrila; Mannenium and European (1999).  Perlman and Butow, "Mobile latrons and intron-Encoded Provines." Science 246:1106 (1989).  Counter, et al., "Detection of siskle well B*-globin allele by hydridization with synthetic diagnoceleotides." Proc. Natl. Acad. Sci. 80:218-282 (1984).  Perlman and Butow, "Mobile latrons and intron-Encoded Provines." Science 246:1106 (1989).  Counter, et al., "Cenetic Attentions During Colorectal-Tumor Development," N. Eng. J. Med. 219:525-532 (1988);  Far et al., "Analysis of RAS gene mutations in acute mycloid leukemia by polymerase chain reaction and oligonacieotide probes," Proc. Natl. Acad. Sci. 81:1620-1631 (1986);  Lyons, et al., "Two G Protein Oncogenes in Human Endocrine Tumora," Science 249:655-659 (1990);  Analysis, "Analysis of RAS gene mutations in acute mycloid leukemia by polymerase chain reaction and oligonacieotide probes," Proc. Natl. Acad. Sci. 82:1620-1631 (1986);  Scholtz, et al., "Analysis of RAS gene mutations in acute mycloid leukemia by polymerase chain reaction and oligonacieotide probes," Proc. Natl. Acad. Sci. 82:1620-1631 (1990);  Analysis, "Analysis of RAS gene mutations in acute mycloid leukemia by polymerase chain reaction and oligonacieotide probes," Proc. Natl. Acad. Sci. 82:1620	INFORMATIO	ON DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary)	Applicant: MARY ANN D. BROW et al	<u></u>		
Dack et al., "Probe Amplifier System Based on Chimanic Cycling Diagonucleosides," #BaTeck, 9:142 (1990);  Uscles et al., "A novel method for the mpid desection of specific necleotide sequences in crude biological samples without blotting @delinearisis application to the acalysis in Remails 9-rate in human secur." One 61:232-2546 (1917).  Gogus et al., "Decection of single base minoralches of thymine and cytosine estitudes by potacic am permanganase and hydrocylamine in the proce of feetablyhumonorium stalis." Noci Acids Res., 13:6807-8817 (1990).  Barlow and Lichach, "Greatesic by gel electrophosesis the impact of pulsed field gel electrophoresis on mammalian genetics," Trands Genet., 3:1 (1987).  Barlow and Lichach, "Greatesic by gel electrophoresis of pulsed field gel electrophoresis on mammalian genetics," Trands Genet., 3:1 (1987).  Bertman and Blutow, "Mobile Instruss and Intron-Emodeld Probins," Science 249-1106 (1989).  Cornect, et al., "Detection of sicile cell Plejabian allele by hybridization with synthetic oligonucleosides," Proc. Natl. Acad. Sci. 80:278-282 (1988).  Fur et al., "Analysis of Refs gene mutations in acute myculad leaterns by polymerase chain reaction and oligonucleoside probes," Proc. Natl. Acids Sci. 80:278-283 (1988).  John Sci. 85:158-1591 (1988).  Aberman et al., "Connecte Acids Deception of Single Base Changes in Human Emoders Circ Champ) to genomic DNA fragments by the polymerase chain reaction reaction of Single-base changes," Proc. Natl. Acids Sci. 80:232-230 (1989).  Learna and Silverstein, "Computational Simulation of DNA Melting and Its Application to Deraturing Gradient Gel Electrophoresis," Natl. Acids Res., 18:2699-2701 (1990).  Warrell or al., "Austhement of a 60-base-pair Grt-Circle sequence (GC-champ) to genomic DNA fragments by the polymerase chain reaction reaction reaction of single-base changes," Proc. Natl. Acids. Sci. 80:232-230 (1989).  Sanifacia, et al., "Acid Method of Decesting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Sol	37 CFR § 1.98(b))	(Ose Several Sheets if Necessary)	Filing Date: 08/28/01	Group Art Unit: 36/626		
12 Dack et al., "Probe Amplifier System Based on Chimeric Cycling Oligonucleonides," BioTeck., 9-162 (1996).  12 Urdea et al., "A novel method for the mpid detection of specific neutodies sequence in crude biological samples without blonking Standardinary application to the analysis of hepatites It virus in human sensem," Cene 61253-264 (1987);  13 Goges et al., "Detection of single base immarkets of thyratine and cyrosine readines by points um permanganate and hydraxylamine in the prese of ternity-Ammentium cells," Mich. Acid. Res., 1807-878-87 (1994);  13 Gomes, et al., "Detection of single base and intron-Encoded Proceius," Science 246-1166 (1989);  24 Pertinas and Butsw. 'Mobile Introns and Intron-Encoded Proceius," Science 246-1166 (1989);  25 Pertinas and Butsw. 'Mobile Introns and Intron-Encoded Proceius," Science 246-1166 (1989);  26 Commer, et al., "Detection of Sciele cell Prigabina allele by hydridatation with synthetic eligamyclooxides," Proc. Natl. Acad. Sci. 83.1639-1631 (1986).  26 Fart et al., "Analysis of RAS gene mutations in acute mycloid leukerma by polymenuse chain searcino and oligonucleositide probes," Proc. Natl. Acad. Sci. 83.1639-1631 (1986).  27 Abamas et al., "Young C Protein Oncogenes in Human Endocrine Tumora," Science 240-55-569 (1990);  28 Abamas et al., "Young C Protein Oncogenes in Human Endocrine Tumora," Science 240-55-569 (1990);  29 Science at al., "Comprehensive Detection of Single Base Changes in Human Genoaite DNA Using Denaturing Gradient Gel Electrophoresis and CC Chang," Genomics 7463-472 (1990).  29 Science at al., "Comprehensive Detection of Single Base Substitutions in Ruman Genoaite DNA Using Denaturing Gradient Gel Electrophoresis and CC Chang." Genomics 7463-472 (1990).  20 Science at al., "Comprehensive Detection of Single Base Substitutions in Ruman Genoaite DNA Using Denaturing Gradient Gel Electrophoresis," Mach. Acad. Sci. USA 88:8405 (1990);  20 Science at al., "Comprehensive Detection of Single Base Substitutions in RNA Molecules by Differential Melting		OTHER DOCUMENTS (Including Author, Title, D	Date, Relevant Pages, Place of Publication)	201		
Urbas or al., "A novel method for the opid depection of specific nucleotide sequences in crude biological samples without blorting application to the analysis if hepatitis 8 vinus in human serum," Gene 61 23-2-64 (1987);  Gogos et al., "Detection of single base rismatches of thyrmine and cytosine residues by potass am permanganate and hydroxylamno in the prese of tenthylammonium solis," Nocl. Acid. No. 4, 18.007-681 (1990);  Bathwa and Batow, "Mobile lamons and inton-Encoded Protein," Science 246-1186 (1989).  22 Perlman and Batow, "Mobile lamons and inton-Encoded Protein," Science 246-1186 (1989).  33 Commer, et al., "Genetic Alterations During Colorectal-Tumor Development," N. Eng. J. Med. 319-525-532 (1988);  34 Vogelscin et al., "Genetic Alterations During Colorectal-Tumor Development," N. Eng. J. Med. 319-525-532 (1988);  35 Fare et al., "Analysis of RAS" gene mutations in acute myeloid leukerma by polymerose chain seaction and oligonucleotide probes," Proc. Natl. Acad. Sci. 86:120-1931 (1988);  36 Lyons, et al., "Two G Protein Oncogenes in Human Endocrine Tumors," Science 249:655-639 (1990);  37 Alamas et al., "Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Grudient Gel Electrophoresis and GC Clamp," Genomics 746-547-57 (1990);  38 Shellied, et al., "Alament of a 60-base-gain GPC with sequence (GC-clamp) to genomic DNA fragments by the polymenas by the polymenas chain reaction reaction reaction and Silversion," Company of Science 249-256 (1989);  39 Lerman et al., "Constant denaturan: gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. 1862-197-1970 (1990);  40 Lerman et al., "Constant denaturan: gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:8405 (1990);  41 Smith et al., "Devel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Mething Behavior in Solution," Genomics 5:17-271-272 (1988);  42 School, et al., "Rapid and Sensitive Detection of Poi	28	Duck et al., "Probe Amplifier System Based on Chimeric Cyclin	ng Oligonucleotides," BioTech., 9:142 (1990);	) )/2(		
Toggs **/ art. **Perceion of single Park monitacines on uniform the process of reinthylymmonium sails." **Nate Acids Res.**, 136867-8817 (1993).  Barlow and Lahrach, "Genetics by gel electrophoresis: the impact of pulsed field gel electrophoresis on mammalian genetics," **Trends Genet.**, 31 (1987).  Perlman and Butow, "Mobile Introns and Intron-Encoded Proteins," **Science 246:1106 (1989).  Counter, et al., "Detection of sickle cell Psylobia alide by hybridization with synthetic dignuscleotides," **Proc. Natl. Acad. Sci. 80:178-282 (1988).  Vogalastin et al., "Genetic Alternations During Colorectal-Tumor Development," **N Eng. J. Med. 319:525-532 (1988).  Tear et al., "Analysis of RAG's gene mutations in acute myeloid leukemia by polymenase chain reaction and oligonucleotide probes," **Proc. Natl. Acad. Sci. 85:1629-1633 (1988).  Lyons, et al., "Two O Protein Oncogenes in Human Endocrine Tumors," **Science 249:655-659 (1990).  Abrains et al., "Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Gradient Gel Electrophosesis and GC Clamp," **Genomic T-403-475 (1990).  Selffield, et al., "Attachment of a 40-base-pair Gr-C-rich sequence (GC-clamp) to genomic DNA fragments by the polymerase chain reaction res in improved detection of single-base changes," **Proc. Natl. Acad. Sci. 80:222-236 (1909).  Leman and Silverstoin, "Computational Simulation of DNA Melting and its Application to Denaturing Gradient Gel Electrophoresis," **Mach. Enzyword, 13548-236 (1907).  Authority of the Computational Simulation of DNA Melting and its Application to Denaturing Gradient Gel Electrophoresis, "**Mach. Enzyword, 13548-236 (1907).  Borrest et al., "Constant denaturan: gel electrophoresis in RNA Molecules by Differential Melting Behavior in Solution," **Cenomics 1317-233 (1988).  Borrest et al., "Constant denaturan: gel electrophoresis as a rapid screening technique for p53 mutations," **Proc. Natl. Acad. Sci. USA (1990).  Contact et al., "Rapid screening for Fp33 mutations by temperature gradien	2000年			<b>5</b>		
132 Perman and guarw, widotic introns and introbe-thouse Process, Series 240 (1982)  333 Conner, et al., "Detection of sickle cell 69-globin allele by alybridization with synthetic eligonucleotides," Proc. Natl. Acad. Sci. 80.278-282 (1983)  344 Vogelstein et al., "Genetic Afterations During Colorectal-Tumor Development," N. Eng. J. Med. 319-525-532 (1983);  355 Fair et al., "Analysis of RAS gens mutations in acute myeloid leukemia by polymenase chain reaction and oligonucleotide probes," Proc. Natl. Acad. Sci. 85-1052-1033 (1988),  356 Lyons, et al., "Two G Protein Oncogenes in Human Endoctine Tumors," Science 249-655-659 (1990);  367 Abrams et al., "Comprehensive Detection of Single Base Changes," Analysis of CC Clamp, and all the Colored		of tetralkylammonium salts " Nucl. Acids Res. 18:6807-6817 (19		ate and hydroxylamine in the presen		
132 Perman and guarw, widotic introns and introbe-thouse Process, Series 240 (1982)  333 Conner, et al., "Detection of sickle cell 69-globin allele by alybridization with synthetic eligonucleotides," Proc. Natl. Acad. Sci. 80.278-282 (1983)  344 Vogelstein et al., "Genetic Afterations During Colorectal-Tumor Development," N. Eng. J. Med. 319-525-532 (1983);  355 Fair et al., "Analysis of RAS gens mutations in acute myeloid leukemia by polymenase chain reaction and oligonucleotide probes," Proc. Natl. Acad. Sci. 85-1052-1033 (1988),  356 Lyons, et al., "Two G Protein Oncogenes in Human Endoctine Tumors," Science 249-655-659 (1990);  367 Abrams et al., "Comprehensive Detection of Single Base Changes," Analysis of CC Clamp, and all the Colored	CATTON TO THE STATE OF THE STAT	Barlow and Lehrach, "Genetics by gel electrophoresis: the impac (1987);	et of pulsed field gel electrophoresis on mamm	nalian genetics," <i>Trends Gene</i> t., 3:16		
Vogelstein et al., "Genetic Alternations During Colorectal-Tumor Development," N. Eng. J. Med. 319:525-332 (1988);  Bert et al., "Analysis of RAS gene mutations in acute mycloid leukemia by polymerase chain reaction and oligonucleotide probes," Proc. Natl. Acad. Sci. 85:1629-1633 (1988);  Lyons, et al., "Two G Protein Oncogenes in Human Endocrine Tumors," Science 249:655-639 (1990);  Abnums et al., "Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Gradient Gel Electrophoresis and Cic Champ," Genomics 7:465-475 (1990);  Schefflick, et al., "Antenmont of a 40-base-pair Gr-Cricin sequence (GC-champ) to genomic DNA fragments by the polymerase chain reaction res in improved detection of single-base changes," Proc. Natl. Acad. Sci., 86:237-226 (1989);  Leman and Silverstein, "Computational Simulation of DNA Melting and Its Application to Denaturing Gradient Gel Electrophoresis," Meth. Engand., 155:482-501 (1987).  Writtell et al., "Detecting base pari substitutions in DNA fragments by temperature-gradient gel electrophoresis," Nucl. Acids Res., 18:2699-2701 (1990).  Bornesen et al., "Constant denaturan: gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:8405 (1991);  Cente. 2:2155 (1993);  Hay al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993);  Genet. 2:2155 (1993);  Hay al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 (1985);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  Wallace et al., "Rapid and Sensitive Detection of Point Mutations of human genetic diseases," Biochimite 67:755 (1985);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461	<i>M</i> 32	Perlman and Butow, "Mobile Introns and Intron-Encoded Protein	ns," Science 246:1106 (1989);			
Farr et al., "Analysis of RAS gene mutations in acute myeloid leukemia by polymerase chain reaction and oligonucleotide probes," Proc. Natl. Acad. Sci. 83:1629-1633 (1988);  Lyons, et al., "Two G Protein Oncogenes in Human Endocrine Tumors," Science 249:655-659 (1990);  Abarms et al., "Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Gradient Gel Electrophoresis and GC Clamp," Genomics 7:463-475 (1990);  Absentied, et al., "Attachment of a 40-base-pair G*C-rich sequence (GC-clamp) to genomic DNA Using Denaturing Gradient Gel Electrophoresis and GC Clamp," Genomics 7:463-475 (1990);  Leman and Silverstein, "Computational Simulation of DNA Melting and its Application to Denaturing Gradient Gel Electrophoresis," Meth. Engineering 1,355-882-591 (1987);  Warnelle of al., "Detecting base pair substitutions in DNA fragments by temperature-gradient gel electrophoresis," Nucl. Acids Res., 18:2699-2701 (1990);  Warnelle of al., "Posted Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," Genomics 3:217-223 (1988);  Bornesen et al., "Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acid. Sci. USA 83:8405 (1991);  Schotz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993);  Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  This are al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 (1975);  This are al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 (1975);  Warnet et al., "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46453 (1960);  Warnet et al., "Strand Separation an	<b>M</b> 33	Conner, et al., "Detection of sickle cell β <sup>s</sup> -globin allele by hybrid	dization with synthetic oligonucleotides," Pro-	c. Natl. Acad. Sci. 80:278-282 (198:		
Lyons, et al., "Two G Protein Oncogenes in Human Endocrine Tumors," Science 249:655-659 (1990);  Abrane al., "Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Gradient Gel Electrophoresis and GC Clamp," Genomics 7:463-473 (1990);  Sheffield, et al., "Attachment of a 40-base-pair Gr-C-rich sequence (GC-clamp) to genomic DNA fragments by the polymerase chain reaction res in improved detection of single-base changes," Proc. Natl. Acad. Sci. 86:232-236 (1989);  Leman and Silverstein, "Computational Simulation of DNA Melting and Its Application to Denaturing Gradient Gel Electrophoresis," Meth. Engangel., 155:482-301 (1987).  Wattell et al., "Detecting base pari substitutions in DNA fragments by temperature-gradient gel electrophoresis," Nucl. Acids Res., 18:2699-2701 (1990).  Wattell et al., "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," Genomics 3:217:223 (1983).  Romesen et al., "Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:3405 (1991).  Scholz, et al., "Rapid ascreening for Tp53 mutations by temperature gradient: gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Const. 22:155 (1993).  Scholz, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 879, (1989).  Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Eingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:431 (1980);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:431 (1980);  Sudencki and Wallace, "Allele-Specific Recombination in Deoxyribonucleic acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1980);  Marmar et	<b>3</b> 4	Vogelstein et al., "Genetic Alterations During Colorectal-Tumor	Development," N. Eng. J. Med. 319:525-532	(1988);		
Abrams et al., "Comprehensive Detection of Single Base Changes in Human Genomic DNA Using Denaturing Gradient Gel Electrophoresis and GC Clarap," Genomics 7:4634-75 (1990);  Sheffield, et al., "Attachment of a 40-base-pair G+C-rich sequence (GC-clamp) to genomic DNA fragments by the polymerase chain reaction res in improved detection of single-base changes," Proc. Natl. Acad. Sci., 36:232-236 (1989);  Lerman and Silverstein, "Computational Simulation of DNA Melting and Its Application to Denaturing Gradient Gel Electrophoresis," Meth. Enzymol., 153:482-501 (1987);  Warnell or al., "Detecting base pari substitutions in DNA fragments by temperature-gradient gel electrophoresis," Nucl. Acids Res., 18:2699-2701 (1990);  Warnell or al., "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," Genomics 3:217-223 (1988);  Bornesen et al., "Constant denaturant: gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:8405 (1991);  43 Scholz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993);  44 Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  45 Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:83 (1980);  46 Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  47 Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  48 Duly et al., "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific	25		eukemia by polymerase chain reaction and oli	gonucleotide probes," Proc. Natl.		
GC Clamp," Genomics 7-661-475 (1990);  Sheffield, et al., "Attachment of a 40-base-pair G+C-tich sequence (GC-tlamp) to genomic DNA fragments by the polymerase chain reaction res in improved detection of single-base changes," Proc. Natl. Acad. Sci., 86:232-236 (1989);  Leman and Silverstein, "Computational Simulation of DNA Melting and Its Application to Denaturing Gradient Gel Electrophoresis," Meth. Enzymol., 155:482-501 (1987);  Wartell et al., "Detecting base pair substitutions in DNA fragments by temperature-gradient gel electrophoresis," Nucl. Acids Res., 18:2699-2701 (1990);  Wartell et al., "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," Genomics 3:217-223 (1988);  Bornesen et al., "Constant denaturan: gel electrophoresis as a mipid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:8405 (1991);  43 Scholz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993) ser.  44 Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  45 Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 879, (1988);  46 Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4-97 (1994);  47 Marmur and Lane, "Srand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  48 Doly et al., "Srand Separation and Specific Recombination in Deoxyribonucleic acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  50 Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum. Proc. and Proc. 12 (1983);  51 Studencki et al., "Discrimination among the Human β <sup>3</sup> , and	M 36	Lyons, et al., "Two G Protein Oncogenes in Human Endocrine T	Tumors," Science 249:655-659 (1990);			
in improved detection of single-base changes," <i>Proc. Natl. Acad. Sci.</i> , 86:232-236 (1989);  Leman and Silverstein, "Computational Simulation of DNA Melting and Its Application to Denaturing Gradient Gel Electrophoresis," <i>Math. Enzymol.</i> , 155:482-591 (1987);  Wartell <i>et al.</i> , "Detecting base pari substitutions in DNA fragments by temperature-gradient gel electrophoresis," <i>Nucl. Acids Res.</i> , 18:2699-2701 (1990);  Smith <i>et al.</i> , "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," <i>Genomics</i> 3:217-223 (1988);  Borreson <i>et al.</i> , "Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations," <i>Proc. Natl. Acad. Sci. USA</i> 88:8405 (1991);  Scholz, <i>et al.</i> , "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," <i>Hum. Mol. Genet.</i> 2:2155 (1993);  Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," <i>PCR Math. Appl.</i> , 1:34-38, (1991);  Orita, <i>et al.</i> , "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," <i>Genomics</i> 5:87 879, (1989);  Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," <i>PCR Methods Appl.</i> , 4:97 (1994);  Mamur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:461 (1960);  Wallace <i>et al.</i> , "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," <i>Biochimie</i> 67:755 (1985);  Studencki at al., "Discrimination among the Human β*, β*, and β*-Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," <i>Human Genetics</i> 37:42 (1985);  Studencki at al., "The Calf 5*- to 3*-Exonuclease is Also an Endonaclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," <i>J. Biol. Chem.</i> 269:1191 (1994);	DD 37		es in Human Genomic DNA Using Denaturing	Gradient Gel Electrophoresis and		
Enzymol., 155-482-501 (1987);  Wartell et al., "Detecting base pari substitutions in DNA fragments by temperature-gradient gel electrophoresis," Nucl. Acids Res., 18:2699-2701 (1990);  Smith et al., "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," Genomics 3:217-223 (1988);  Bornesen et al., "Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:8405 (1991);  43 Scholz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993);  44 Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  45 Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 879, (1989);  46 Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  47 Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:463 (1960);  48 Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic decides: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  49 Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  50 Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Human Genetic 37:42 (1985);  51 Studencki et al., "Discrimination among the Human β <sup>A</sup> , β <sup>A</sup> , and β <sup>C</sup> -Globin Genes Using Allele-Specific Phybridization Probes," Human Genetic 37:42 (1985);  52 Marante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 26	38			y the polymerase chain reaction res		
Smith et al., "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," Genomics 3:17-223 (1988);  Borresen et al., "Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations," Proc. Natl. Acad. Sci. USA 88:8405 (1991);  Scholz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993);  Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 879, (1989);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  Wallace et al., "Strand Separation and Specific Recombination in Deoxyribonucleic decids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimic 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Human Genetics 37-42 (1985);  Studencki et al., "Discrimination among the Human β <sup>3</sup> , β <sup>3</sup> , and β <sup>6</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37-42 (1985);  Murante et al., "The Call 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	39		lting and Its Application to Denaturing Gradie	ent Gel Electrophoresis," Meth.		
Borresen et al., "Constant denaturant gel electrophoresis as a rapid screening technique for p53 mutations," <i>Proc. Natl. Acad. Sci. USA</i> 88:8405 (1991);  Scholz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," <i>Hum. Mol. Genet.</i> 2:2155 (1993);  Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," <i>PCR Meth. Appl.</i> , 1:34-38, (1991);  Ortia, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," <i>Genomics</i> 5:87 879, (1989);  Hammur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:453 (1960);  Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," <i>Biochimie</i> 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum β <sup>Δ</sup> - and β <sup>Δ</sup> -Globin Genes," <i>DNA</i> 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>Δ</sup> , β <sup>Δ</sup> , and β <sup>C</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," <i>Human Genetics</i> 37:42 (1985);  Murante et al., "The Calf 5 <sup>+</sup> - to 3 <sup>+</sup> -Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," <i>J. Biol. Chem.</i> 269:1191 (1994);	40		nts by temperature-gradient gel electrophoresis	s," Nucl. Acids Res., 18:2699-2701		
Scholz, et al., "Rapid screening for Tp53 mutations by temperature gradient gel electrophoresis: a comparison with SSCP analysis," Hum. Mol. Genet. 2:2155 (1993);  44 Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  45 Oria, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 (1989);  46 Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  47 Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  48 Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  49 Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  50 Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum. β <sup>h</sup> . and β <sup>h</sup> -Globin Genes," DNA 3:1 (1984);  51 Studencki et al., "Discrimination among the Human β <sup>h</sup> , β <sup>h</sup> , and β <sup>c</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  52 Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  53 Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	<b>1</b> 41		ons in RNA Molecules by Differential Melting	g Behavior in Solution,"Genomics		
Genet. 2:2155 (1993);  Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detection of Mutations in the Genomic DNA," PCR Meth. Appl., 1:34-38, (1991);  Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87 879, (1989);  Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Human β <sup>Δ</sup> and β <sup>β</sup> -Globin Genes," DNA 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>Δ</sup> , β <sup>β</sup> , and β <sup>c</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	13 42		id screening technique for p53 mutations," Pr	oc. Natl. Acad. Sci. USA 88:8405		
Orita, et al., "Rapid and Sensitive Detection of Point Mutations and DNA Polymorphisms Using the polymerase Chain Reaction," Genomics 5:87, (1989);  Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  Mammur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);  Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum β*- and β*-Globin Genes," DNA 3:1 (1984);  Studencki et al., "Discrimination among the Human β*, β*, and β*-Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5*- to 3*-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	2 43	Scholz, et al., "Rapid screening for Tp53 mutations by temperatu Genet. 2:2155 (1993);	are gradient gel electrophoresis: a comparison	with SSCP analysis," Hum. Mol.		
1879, (1989);  Liu and Sommer, "Parameters Affecting the Sensitivity of Dideoxy Fingerprinting and SSCP," PCR Methods Appl., 4:97 (1994);  Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA (46:453 (1960);  Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA (46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum β <sup>Δ</sup> - and β <sup>S</sup> -Globin Genes," DNA 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>Δ</sup> , β <sup>S</sup> , and β <sup>C</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	<i>2</i> 44	Hayashi, "PCR-SSCP: A Simple and Sensitive Method for Detec	ction of Mutations in the Genomic DNA," PC	CR Meth. Appl., 1:34-38, (1991);		
Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:453 (1960);  Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," <i>Biochimie</i> 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum β <sup>Λ</sup> - and β <sup>S</sup> -Globin Genes," <i>DNA</i> 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>Λ</sup> , β <sup>S</sup> , and β <sup>C</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," <i>Human Genetics</i> 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," <i>Genes and Develop</i> . 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," <i>J. Biol. Chem.</i> 269:1191 (1994);	<b>1</b> 45		and DNA Polymorphisms Using the polymera.	se Chain Reaction," Genomics 5:87		
46:453 (1960);  Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum β <sup>5</sup> - and β <sup>5</sup> -Globin Genes," DNA 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>5</sup> , β <sup>5</sup> , and β <sup>c</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	46	Liu and Sommer, "Parameters Affecting the Sensitivity of Dideo	xy Fingerprinting and SSCP," PCR Methods	Appl., 4:97 (1994);		
46:461 (1960);  Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);  Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Humβ^- and β <sup>s</sup> -Globin Genes," DNA 3:1 (1984);  Studencki et al., "Discrimination among the Human β^, β <sup>s</sup> , and β <sup>c</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	17) 47	Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," Proc. Natl. Acad. Sci. USA 46:453 (1960);				
Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Hum β <sup>A</sup> - and β <sup>S</sup> -Globin Genes," DNA 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>A</sup> , β <sup>S</sup> , and β <sup>C</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	AS) 48	Doty et al., "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemical Studies," Proc. Natl. Acad. Sci. USA 46:461 (1960);				
β <sup>A</sup> - and β <sup>S</sup> -Globin Genes," <i>DNA</i> 3:1 (1984);  Studencki et al., "Discrimination among the Human β <sup>A</sup> , β <sup>S</sup> , and β <sup>C</sup> -Globin Genes Using Allele-Specific Oligonucleotide Hybridization Probes," <i>Human Genetics</i> 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," <i>Genes and Develop.</i> 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," <i>J. Biol. Chem.</i> 269:1191 (1994);	. 13 49	Wallace et al., "Application of synthetic oligonucleotides to the diagnosis of human genetic diseases," Biochimie 67:755 (1985);				
Human Genetics 37:42 (1985);  Harrington and Liener, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	50	Studencki and Wallace, "Allele-Specific Hybridization using Oligonucleotide Probes of Very High Specific Activity: Discrimination of the Human β <sup>A</sup> - and β <sup>S</sup> -Globin Genes," DNA 3:1 (1984);				
nucleotide excision repair," Genes and Develop. 8:1344 (1994);  Murante et al., "The Calf 5'- to 3'-Exonuclease Is Also an Endonuclease with Both Activities Dependent on Primers Annealed Upstream of the Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	51					
Point of Cleavage," J. Biol. Chem. 269:1191 (1994);	<i>M</i> 52					
aminer: William Sandyl Date Considered: 6-10-07	3 53		onuclease with Both Activities Dependent on	Primers Annealed Upstream of the		
	aminer: 41/,	lian Souls	Date Considered: 6-10-0	7		



6-10.03

Date Considered:

80

Examiner:

Science 260:819 (1993);

FORM PTO-1449 (Modified)

U.S. Department of Commerce Patent and Trademark Office

Attorney Docket No.: FORS-06612

Serial No.: 09/940,925

Applicant: MARY ANN D. BROW et al.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary)

(37 CFR § 1.9	98(b))		Filing Date: 08/28/01	Group Art Unit: (636 %			
		OTHER DOCUMENTS (Including Author, Title, Da	ate, Relevant Pages, Place of Publication)	03			
	81	Shinnick and Jones in Tuberculosis: Pathogenesis, Protection D.C., pp. 517-530 (1994);	and Control, Bloom, ed., American Society	y of Microbiology, Washington,			
2020	₩ 82	Yule, "Amplification-Based Diagnostics Target TB," Bio/Technology 12:1335 (1994);					
JAM	83	Heym et al., "Implications of multidrug resistance for the future 344:293 (1994);	e of short-course chemotherapy of tubercule	osis: a molecular study," Lancet			
THI & TRADE	84	Morris et al., "Molecular Mechanisms of Multiple Drug Resista 171:954 (1995);	nce in Clinical Isolates of Mycobacterium	tuberculosis," J. Infect. Dis.			
11)	85	Banerjee et al., "inhA, a Gene Encoding a Target for Isoniazid	and Ethionamide in Mycobacterium tubero	culosis," Science 263:227 (1994);			
	86_	Woese, "Bacterial Evolution," Microbiological Reviews, vol 51	, No. 2. (1987);				
111	87	Shibata, "Preparation of Nucleic Acid for Archival Material," i Boston, pp. 47-54 (1994);	n PCR: The Polymerase Chain Reaction,	Mullis et al., eds. Birkhauser,			
A	88	Saiki et al., "Primer-Directed Enzymatic Amplification of DNA	with a Thermostable DNA Polymerase,"	Science 239:487 (1988);			
m	89	Mullis and Faloona, "Specific Synthesis of DNA in Vitro via a (1987);	Polymerase-Catalyzed Chain Reaction," M	fethods in Enzymology 155:335			
2	90	M. Bargseid et al., "A High Fidelity Thermostable DNA Polyn CA) 4:34 (1991);	nerase Isolated from Pyrococcus furiosus,"	Strategies (Startagene, LaJolla,			
1	91	Perler et al., "Intervening sequences in an Archaea DNA polyr	nerase gene," Proc. Natl. Acad. Sci. USA 8	39:5577 (1992);			
B	92	Kaledin et al., "Isolation and Properties of DNA Polymerase F 46:1576 (1981);	rom the Extremely Thermophilic Bacteriun	n Thermus flavus," Biokhimiya			
	93	Carballeira et al., "Purification of a Thermostable DNA Polymer Reaction," Biotechniques 9:276 (1990);	erase from Thermus thermophilus HB8, Us	eful in the Polymerase Chain			
1	94	Myers et al., "Reverse Transcription and DNA amplification by	y a Thermus thermophilus DNA Polymeras	e," Biochem. 30:7661 (1991);			
- Th	95	Ito et al., "Compilation and alignment of DNA polymerase seq	uences," Nucl. Acids Res. 19:4045 (1991);				
	96	Mathur et al., The DNA polymerase gene from the hypertherm homology with α-like DNA polymerases," Nucl. Acids. Res. 19	nophilic marine archaebacterium <i>Pyrococcu</i> 9:6952 (1991);	s furiosus, shows sequence			
13	97	Dunn et al., "Complete Nucleotide Sequence of Bacteriophage (1983);	T7 DNA and the Locations of T7 Genetic	Elements," J. Mol. Biol. 166:477			
m	98	Antao et al., "A thermodynamic study of unusually stable RNA	and DNA hairpins," Nucl. Acids Res. 19:	5901 (1991);			
M	99	Stark, "Multicopy expression vectors carrying the <i>lac</i> repressor 5:255 (1987);	gene for regulated high-level expression o	f genes in Escherichia coli," Gene			
17	100	Studier and Moffatt, "Use of Bacteriophage T7 RNA Polymera 189:113 (1986);	se to Direct Selective High-level Expressio	n of Cloned Genes," J. Mol. Biol.			
m	101	Sambrook et al., Molecular Cloning. A Laboratory Manual, C (1989);	old Spring Harbor Laboratory Press, Cold	Spring Harbor, pp. 1.63-1.69			
M	102	Engelke, "Purification of Thermus Aquaticus DNA Polymerase	Expressed in Escherichia coli," Anal. Bioc	chem 191:396 (1990);			
	103	Copley and Boot, "Exonuclease Cycling Assay: An Amplified (1992);	Assay for the Detection of Specific DNA	Sequences," BioTechniques 13:888			
B	104	King, R.A., et al., "Non-random Distribution of Missense Mutarelated)Oculocutaneous Albinism," Mol. Biol. Med. 8:19 (1991)	itions Within the Human Tyrosinase Gene	in Type 1 (Tyrosinase-			
1/2	105	Giebel et al., "Organization and Nucleotide Sequences of the Human Tyrosinase Gene and a Truncated Tyrosinase-Related Segment," Genomics 9:435 (1991);					
6/1	106	Spritz, "Molecular genetics of oculocutaneous albinism," Huma	n Molecular Genetics 3:1469 (1994);				
Examiner:	U	villia Salpse	Date Considered: 6-10-67				
EXAMINER:	lnit wit	tial citation considered. Draw line through citation if not in confe h next communication to applicant.	ormance and not considered. Include copy	of this form			



U.S. Department of Commerce

Patent and Trademark Office



Serial No.: 09/940,925

Applicant: MARY ANN D. BROW et al.

Attorney Docket No.: FORS-06612

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary)

FCRM PTO-1449

(Modified)

Group Art Unit: / 6 3 4 Filing Date: 08/28/01 (37 CFR § 1.98(b)) OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication) Giebel et al., "A Tyrosinase Gene Missense Mutation in Temperature-sensitive Type I Oculocutaneous Albinism," J. Clin. Invest. 87:1119 107 E Bouchard et al., "Induction of Pigmentation in Mouse Fibroblasts by Expression of Human Tyrosinase cDNA," J. Exp. Med. 169:2029 108 Orkin and Kazazian, "The Mutation and Polymorphism of the Human \(\beta\)-Globin Gene and its Surrounding DNA," Annu. Rev. Genet. 18:13 109 (1984);Collins and Weissman, "The Molecular Genetics of Human Hemoglobin," Prog. Nucleic Acid Res. Mol. Biol. 31:315 (1984); 110 Lawn et al., "The Nucleotide Sequence of the Human β-Globin Gene," Cell 21:647 (1980); 111 Orkin and Goff, "Nonsense and Frameshift Mutations in β<sup>0</sup>-Thalassemia Detected in Cloned β-Globin Genes," J. Biol. Chem. 256:9782 112 Goldsmith et al., ""Silent" nucleotide substitution in a β\*-thalassemia globin gene activates splice site in coding sequence RNA," Proc. Natl. 113 Acad. Sci. USA 80:2318 (1983); Giddings et al., "An adaptive, object oriented strategy for base calling in DNA sequence analysis," Nucl. Acids Res. 21:4530 (1993); 114 Trivedi et al., "Selective Amplification of Simian Immunodeficiency Virus Genotypes after Intrarectal Inoculation of Rhesus Monkeys," 115 Journal of Virology 68:7649 (1994); Nugent et al., "Characterization of the Apurinic Endonuclease Activity of Drosophila Rrpl," Biochemistry, 32:11445 (1993); 116 Bardwell et al., "Specific Cleavage of Model Recombination and Repair Intermediates by the Yeast Rad1-Rad10 DNA Endonuclease," 117 Science 265:2082 (1994); Orkin et al., "Abnormal RNA processing due to the exon mutation of \( \beta^E\)-globin gene," Nature, 300:768 (1982); 118 Spritz et al., "Base substitution in an intervening sequence of a β'-thalassemic human globin gene," Proc. Natl. Acad. Sci. USA, 78:2455 119 (1981);120 Baker et al., "Suppression of Human Colorectal Carcinoma Cell Growth by Wild-Type p53," Science 249:912 (1990); Chen et al., "Genetic Mechanisms of Tumor Suppression by the Human p53 Gene," Science 250:1576 (1990); 121 Hollstein et al., "p53 Mutations in Human Cancers," Science 253:49 (1991); 122 Caron de Fromental and Soussi, "TP53 Tumor Suppressor Gene: A Model for Investigating Human Mutagenesis," Genes, Chromosomes 123 and Cancer 4:1 (1992). Inchauspe et al., "Use of Conserved Sequences from Hepatitis C Virus for the Detection of Viral RNA in Infected Sera by Polymerase Chain 124 Reaction," *Hepatology* 14:595 (1991); 125 Miller et al., "The rpoB Gene of Mycobacterium tuberculosis," Antimicrob. Agents Chemother., 38:805 (1994); Cockerill et al., "Rapid Identification of a Point Mutation of the Mycobacterium tuberculosis Catalase-Peroxidase (katG) Gene Associated 126 with Isoniazid Resistance," J. Infect. Dis. 171:240 (1995); Greisen et al., "PCR Primers and Probes for the 16S rRNA Gene of Most Species of Pathogenic Bacteria, Including Bacterial Found in 127 Cerebrospinal Fluid," J. Clin. Microbiol. 32:335 (1994); Widjojoatmondio et al., "Rapid Identification of Bacteria by PCR-Single-Strand Conformation Polymorphism," J. Clin. Microbiol. 32:3002 128 (1994);129 Maidak et al., "The Ribosomal Database project," Nucleic Acids Res., 22:3485 (1994); 130 McConlogue et al., "Structure-independent DNA amplification by PCR using 7-deaza-2'-deoxyguanosine," Nucleic Acids Res. 16:20 (1988); D.S. Sigman et al., "Chemical Nucleases," Chemical Reviews 93:2295-2316 (1993); 131 T.R. Cech et al., "Secondary Structure of the Tetrahymena Ribosomal RNA intervening sequence, Structural homology with fungal 132 mitochondrial intervening sequences," Proc. Natl. Acad. Sci. USA 80:3903 (1983); Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

JAN 3 0 2003

TECH CENTER 1600/2900 Examiner: **EXAMINER:** 



U.S. Department of Commerce Patent and Trademark Office

Attorney Docket No.: FORS-06612

Serial No.: 09/940,925

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

FORM PTO-1449

(Modified)

(Use Several Sheets If Necessary)

Applicant: MARY ANN D. BROW et al.

(37 CFR § 1.98	8(b))		Filing Date: 08/28/01	Group Art Unit: / 6 3 (		
EVC		OTHER DOCUMENTS (Including Author, Tit	le, Date, Relevant Pages, Place of Publi	cation)		
	133	C.R. Woese et al., "Detailed Analysis of the Higher Order Structure of 16S Like Ribosomal Ribonucleic Acids," Microbiology Reviews 47:621 (1983);				
130/	134	Hoheisel et al., "On The Activities of Escherichia coli E	konuclease III," Anal. Biochem. 209:238	3-246 (1993);		
14	135	R. Youil et al., "Screening for Mutations by Enzyme Mis	smatch Cleavage with T4 Endonuclease	VII," Proc. Natl. Acad. Sci. USA (1995);		
TARNO	136	Murphy et al., "Use of the 5' Noncoding Region for Ger	otyping Hepatitis C Virus," J. Infect. Di	iseases 169:473 (1994).		
(0)	137	Takada et al., "HCV genotypes in different countries," Le	ancet 339:808 (1992).			
1/3	138	Belkum, "DNA Fingerprinting of Medically Important M	icroorganisms by Use of PCR," Clin. M	icrobiol. Rev. 7(2): 174-184 (1994).		
	139	Wilson et al., "Amplification of Bacterial 16S Ribosomal (1990).	DNA with Polymerase Chain Reaction,	" J. Clin. Microbiol. 28(9):1942-1946		
113	140	Bingen et al., "Use of Ribotyping in Epidemiological Sur	veillance of Nosocomial Outbreaks," Cl	in. Microbiol. Rev. 7(3):311-327 (1994).		
113	141	Tabor et al., "Effect of Manganese Ions On The Incorpor Escherichia coli DNA Polymerase I, Proc. Natl. Acad. S		ophage T7 DNA Polymerase and		
09	142	Lyamichev <i>et al.</i> , "Structure-specific endonucleolytic clean (1993)	avage of nucleic acids by eubacterial DN	NA polymerases," Science 260:778-783		
My	143	Seela et al., "7-deazapurine containing DNA: efficiencty amplification and protection from endodeoxyribonuclease				
19	144	Young et al., "Detection of hepatitis C virus RNA by a c 31(4) 882-886 (1993)	ombined reverse transcription-polymeras	se chain reaction assay," J. Clin. Microbio		
Examiner:	(4)	Wian Souds	Date Considered:	0-07		
EXAMINER:		tial citation considered. Draw line through citation if not in the next communication to applicant.				

**RECEIVED** JAN 3 0 2003 **TECH CENTER 1600/2900**